Remarks

The Office Action mailed 10 August 2004 has been received and reviewed. Claims 1, 8, and 15 having been amended, the pending claims are claims 1-41. Claims 24-41 being withdrawn from examination as drawn to non-elected inventions, the claims currently under examination are 1-23. Reconsideration and withdrawal of the rejections are respectfully requested.

Support for the claim amendments is found throughout the specification. Support for the recitation "wherein the at least one antibody which is immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4 does not cross-react with other non-usherin proteins within the biological sample" in claims 1, 8, 15 is found, for example, on page 17, line 29 to page 18, line 1 and page 18, lines 17-18 of the specification. Support for the recitation "wherein the biological sample is from a tissue that normally includes the usherin protein in an individual not having Usher syndrome Type IIa" in claims 1, 8, and 15 is found, for example, on page 16, line 2 and page 19, lines 23-5 of the specification.

Restriction Requirement

Applicant notes with appreciation the Examiner's withdrawal of the restriction requirement with regard to group II and the rejoinder and examination of claims 8-14.

The 35 U.S.C. §112, First Paragraph, Written Description Rejection

The Examiner rejected claims 1-23 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserted that although independent claims 1, 8, and 13 are drawn to "antibodies reactive with at least a portion of a human usherin protein having SEQ ID NO:4 . . . the specification, however, . . . has only disclosed antibodies immunoreactive with SEQ ID NOs:1, 2, and 4, and has only provided working examples of antibodies immunoreactive with SEQ ID NOs:1 and 2" (page 4, Office Action mailed August 10, 2004). Asserting that "different antibodies would be capable of being immunoreactive with portions of the human usherin protein, and not be immunoreactive with

SEQ ID NOs:1 and 2," the Examiner asserted the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention (pages 3-4, Office Action mailed August 10, 2004). Applicant respectfully disagrees and traverses this rejection.

"To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" (M.P.E.P. § 2163). "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991)." See M.P.E.P. § 2163.

There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed (Wertheim, 541 F.2d at 262, 191 USPQ at 96) and, generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). See M.P.E.P. § 2163.

Applicant submits that the level of skill in the art of immunology and antibody production is very high. See, for example, U.S. Patent No. 6,692,920 and 6,660,485. Both polyclonal and monoclonal antibodies may be generated to a protein, such as the human usherin protein (SEQ ID NO:4), or any fragment or oligopeptide thereof, using methods that are well known in the art (U.S. Patent No. 6,660,485, col. 21, lines 17-45, and U.S. Patent No. 6,692,920,

col. 8, lines 14-40). For the production of polyclonal antibodies, various hosts including goats, rabbits, rats, mice, humans, and others, may be immunized by injection with the protein, fragment, or oligopeptide thereof. Depending on the host species, various adjuvants may be used to increase immunological response. Monoclonal antibodies may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. Various immunoassays for screening to identify antibodies having a specificity for the immunizing polypeptide are well known in the art (U.S. Patent No. 6,660,485, col. 22, lines 20-31).

Claims 1-23 are drawn to antibodies which are "immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4." The specification describes the complete amino acid sequence of the human usherin protein (SEQ ID NO:4). As described in the specification, an antibody is immunoreactive to human usherin when the antibody recognizes and binds to a site within the SEQ ID NO:4 polypeptide (page 10, lines 10-15 of the specification). As discussed above, methods for generating antibodies to the human usherin protein (SEQ ID NO:4), and any fragments or oligopeptides thereof, are well known in the art. Techniques for determining if an antibody is immunoreactive with a portion of a polypeptide are well know within the art (page 9, line 27 to page 10, line 2 and page 10, lines 19-23), and the specification describes many such immunoassays for determining if an antibody is immunoreactive with the human usherin protein (see, for example, page 18 , lines 12-25 of the specification). Finally, the specification provides two working examples of antibodies that are "immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4;" one, an antibody immunoreactive to the twenty-three amino acid sequence of SEQ ID NO:1 and, two, an antibody immunoreactive to SEQ ID NO:2, which represents amino acids 318 to 518 of the human usherin protein (SEQ ID NO:4) (see page 22, line 19 to page 23, line 5 of the specification).

Applicant submits that these teachings provide adequate written description for antibodies "immunoreactive with at least a portion of a human usherin protein having SEQ ID

NO:4." Withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

The 35 U.S.C. §112, First Paragraph, Enablement Rejection

The Examiner rejected claims 1, 8, and 15 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. This rejection is traversed.

Specifically, the Examiner asserted that the specification "does not specify what portion and how large a portion of the human usherin protein with which the antibody is reactive" (page 4, Office Action mailed August 10, 2005) and asserted that the "applicants fails to specify any epitopes, nor does the applicant teach how to create antibodies that would be capable of binding to the epitopes in the protein with high affinity, rendering it unclear how a person of ordinary skill in the art would be able to do so" (page 5, Office Action mailed August 10, 2005). Applicant disagrees. Claims 1-23 are drawn to antibodies which are "immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4." The specification describes the complete amino acid sequence of the human usherin protein (SEQ ID NO:4). And, as discussed above, in the response to the written description rejection under 35 U.S.C. §112, first paragraph, methods for making antibodies to a protein and any fragments or oligopeptides thereof, including antibodies to the human usherin protein (SEQ ID NO:4) and any fragments or oligopeptides of the human usherin protein, are well known to the skilled artisan. Thus, Applicant submits that the specification provides adequate guidance to allow one of skill in the art to make and use the method of claims 1-23. Further, Applicant submits that, given that the level of skill in the art of immunology and antibody production is high, the Examiner is inappropriately requiring the Applicant to teach that which is well known to one of ordinary skill in the art.

The Examiner asserted that antibodies "immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4" would also be immunoreactive with other extracellular matrix proteins and cell adhesion molecules in the sample, thus generating false negatives (page 5, Office Action, mailed August 10, 2004). Applicant disagrees, but submit that

in view of the amendment of claims 1, 8, and 15 to recite "wherein the at least one antibody which is immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4 does not cross-react with other non-usherin proteins within the biological sample," this concern is moot.

On page 5 of the Office Action mailed August 10, 2005, the Examiner asserted that the specification "states that the methods of the present invention also provide for the use of antibodies that are immunoreactive with the usherin protein . . . as well as other polypeptides. If the antibody forms an immunoconjugate with other polypeptides, false negatives would potentially be generated." Applicant does not understand the relevance of this assertion to claims 1-23. Claims 1-23 recite "at least one antibody which is immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4 . . . wherein the antibody which is immunoreactive with at least a portion of a human usherin protein having SEQ ID NO:4 does not cross-react with other non-usherin proteins within the biological sample." While the specification might make mention of antibodies that are immunoreactive to proteins other than human usherin, the antibodies of claims 1-23 do "not cross-react with other non-usherin proteins within the biological sample." The Examiner appears to be inappropriately reading the specification into the claims.

The Examiner asserted that, as the specification discloses it "is likely some percentage of individuals with Usher syndrome Type IIa continue to express immunoreactive usherin in their tissues," the accuracy of the claimed methods is unclear. Applicant disagrees. Claims 1-7 and 15-23 are drawn to methods of "determining whether an individual has or is at risk for developing Usher syndrome Type IIa" wherein "the absence of the [antibody-usherin] immunoconjugate [correlates] with the individual having or being at risk for developing Usher syndrome Type IIa." The claimed methods evaluate for the absence of an antibody-usherin protein immunoconjugate and correlate such an absence with the individual having or being at risk for developing Usher syndrome type IIa. The claimed methods will identify individuals with Usher syndrome Type IIa who do not express immunoreactive usherin in their tissues. That additional diagnostic tests will be needed to detect that percentage of individuals with Usher

syndrome Type IIa who continue to express immunoreactive usherin in their tissues does not negate diagnostic capabilities of the claimed methods. Further, Applicant submits that claims 8-14 are drawn to a "method for detecting the presence or absence of an usherin protein." Applicant submits that some individuals suffering from Usher syndrome Type IIa might continue to express the usherin protein is of no relevance.

Finally, the Examiner asserted that, as usherin might have a limited tissue distribution, the claimed method will generate false positives when biological samples that do not normally include human usherin are tested (pages 6-7, Office Action mailed August 10, 2004). Applicant submits that this concern is moot in view of the amendment of claims 1, 8, and 15 to recite "wherein the biological sample is from a tissue that normally includes the usherin protein in an individual not having Usher syndrome Type IIa."

In view of the above discussion, Applicant respectfully submits that the specification provides adequate teaching and guidance for the claimed methods. Reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully requested.

Summary

It is respectfully submitted that the pending claims 1-23 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 9th day of November, 2004, at 11:20 AM (Central Time).

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